Kinetic Studies on the Dealkylation of Esters of Phosphorous, Phosphoric, and Phosphonic Acid. Part I. Dealkylation by Hydrogen Bromide in Ether.

By V. F. G. COOKE and W. GERRARD.

[Reprint Order No. 6101.]

The kinetics of the dealkylation of diethyl hydrogen phosphite, triethyl phosphate, an acetylphosphonate, and alkylphosphonates by hydrogen bromide in ether have been measured. They are consistent with replacement of the first and the second alkyl group by successive reactions each of the second order with respect to the reactants. The rate constants have been evaluated, and provide quantitative measures of the variation in rate with variation of the alkyl groups R and R' in phosphonates, O:PR(OR')₂; they indicate the degree of control available in the preparation of esters of the type O:PR(OR')·OH, O'PH(OR')·OH, and O'P(OR')₂·OH.

An important feature of alkyl phosphites, phosphates, and phosphonates is their dealkylation by hydrogen halides, which remove alkyl groups as alkyl halide. Qualitative studies have previously been made by Gerrard (J., 1940, 1464; 1944, 85; 1945, 848), Cooke, Gerrard, and Green (*Chem. and Ind.*, 1953, 351), Gerrard, Green, and Nutkins (J., 1952, 4076), and Gerrard, Isaacs, Machell, Smith, and Wyvill (J., 1953, 1920), and kinetic studies were initiated by Gerrard and Whitbread (J., 1952, 914) who showed that the rates of successive removal of alkyl groups from tri-*n*-butyl phosphite were in the order 1st $\geq 2nd >$ 3rd, for a given hydrogen halide, and that for each group the rates were in the order HI > HBr > HCl.

The measurements of rates of dealkylation of a number of esters of the type $O:PR'(OR)_2$ were undertaken to generalise the kinetic technique for such consecutive reactions, to elucidate mechanisms of dealkylation, to indicate conditions for the preparation of acid esters, and to reveal to what extent electronic influence is transmitted through the phosphorus atom.

Rate measurements reveal that the main reactions studied are (a) and (b). These are competitive consecutive reactions in which the material measured is consumed in each.

(a) $O:PR'(OR)_2 + HBr \longrightarrow O:PR'(OR) \cdot OH + RBr$

(b) $O:PR'(OR) \cdot OH + HBr \longrightarrow O:PR'(OH)_{s} + RBr$

A strict mathematical solution of general applicability has not yet been devised. Frost and Schwemer (J. Amer. Chem. Soc., 1952, 74, 1268), however, provided an analysis for the case where the reactants are stoicheiometrically equivalent. Their purpose was to integrate this kinetic system in terms of general variables which could be applied to experimental results for this class of reaction, and they tested their procedure on the hydrolysis of ethyl adipate and succinate. When the ratio of the rate constants k_1/k_2 is more than 10 the following method is easier and is not restricted to equimolecular concentrations.

Evaluation of Specific Rate Constants, k_1 and k_2 .—When $k_1 > 10k_2$, let a_0 be the initial concentration of hydrogen bromide, b_0 be the initial concentration of the ester, a and b the concentration at time t, and c the concentration of the half ester, then

$$-\mathrm{d}a/\mathrm{d}t = k_1 a b + k_2 a c \qquad . \qquad . \qquad . \qquad . \qquad . \qquad (1)$$

When $k_1 > 10k_2$, for a measurable initial extent of reaction, the approximate equation (2) holds sufficiently accurately to allow evaluation of k_1 :

by the usual integrated expression for such a second-order equation. For the later stages of reaction, the following approximate equation becomes progressively more applicable :

If a' is the hydrogen bromide consumed by the first dealkylation and a'' that by the second in time t, then

and at later stages $a' \approx b_0$.

Hence

Integrating, we have :

For the special case of initially equimolecular concentrations $a_0 = 2b_0$, we have

It is also possible to extend Frost and Schwemer's tables (*loc. cit.*) for cases where $k_1 > 10k_2$. This laborious procedure was performed and compared for typical cases with the method given above. The equality of results demonstrated the reliability of the methods.



The middle part of the reaction curve was not used in evaluation of rate constants when $k_1/k_2 > 10$. It is worth investigating if the values of k_1 and k_2 do supply a calculated rate in this region in agreement with experiment. This can be done by utilising Frost and Schwemer's equation (7):

where $\beta = b/b_0$, $\kappa = k_2/k_1$ and $\tau = b_0k_1t$. For κ determined from initial and final stages, graphical integration of (7) for various values of β was performed to give corresponding values of τ . For each value of β , the value of $\alpha = a/a_0$ was found by Frost and Schwemer's equation (10):

$$lpha = [(1-2\kappa)/2(1-\kappa)]eta + [1/2(1-\kappa)]eta^{\kappa}$$

Hence, since α and τ are known, a calculated line of α versus t could be drawn for appropriate values of a_0 . The fit was very satisfactory (see Figure).

Frost and Schwemer's analysis was devised to obtain rate constants for cases where $k_1 < 10k_2$. The times required to reach specified extents of reaction are measured, and several ratios taken, *e.g.*, the times required for 60% and for 30% reaction. These ratios are obviously dependent on the relative values of k_1 and k_2 . Tables are provided for using these ratios and absolute times of reaction so as enable k_1 and k_2 to be read off. For various ratios, with one initial equimolecular concentration and for various initial equimolecular concentrations, constant values for k_1 and k_2 were obtained for the stepwise dealkylations mentioned.

EXPERIMENTAL

Preparation of Esters.—Dialkyl alkylphosphonates were prepared from the corresponding trialkyl phosphites and an alkyl halide, by the Arbuzov reaction (J. Russ. Phys. Chem. Soc., 1906, **38**, 687) and were purified by careful fractionation. Diethyl ethylphosphonate had b. p. $82^{\circ}/10 \text{ mm.}, n_{2}^{\circ}$ 1.4168 (Found : P, 18.75. Calc. for $C_{6}H_{15}O_{3}P$: P, 18.7%). Diethyl *n*-octylphosphonate had b. p. $83^{\circ}/0.02 \text{ mm.}, n_{D}^{28}$ 1.4353 (Found : P, 12.4. Calc. for $C_{12}H_{27}O_{3}P$: P,

12·4%). Diethyl 1-phenylethylphosphonate (prepared as described by Gerrard and Green, loc. cit.) had b. p. 88°/0·05 mm., n_D^{18} 1·4870 (Found : P, 12·7. Calc. for $C_{18}H_{19}O_3P$: P, 12·8%). Di-n-propyl ethylphosphonate had b. p. 112°/15 mm., n_D^{20} 1·4238 (Found : C, 49·5; H, 9·80; P, 16·0. $C_8H_{19}O_3P$ requires C, 49·5; H, 9·85; P, 15·95%). Diisopropyl ethylphosphonate had b. p. 90°/19 mm., n_D^{20} 1·4122 (Found : P, 16·1. $C_8H_{19}O_3P$ requires P, 15·95%). Diethyl acetyl-phosphonate, b. p. 110°/17 mm., n_D^{17} 1·4240 (Found : P, 17·25. Calc. for $C_6H_{13}O_4P$: P, 17·2%), was prepared by Kabachnik and Rossiiskaya's method (Isvest. Akad. Nauk, S.S.S.R., Otdel. Khim. Nauk, 1945, 364), but our yield of 78% was considerably better than theirs. Diethyl hydrogen phosphite, b. p. 82°/18 mm., n_D^{18} 1·4100 (Found : P, 22·6. Calc. for $C_4H_{11}O_3P$: P, 22·45%), was prepared as described by Gerrard (J., 1940, 1464). Triethyl phosphate had b. p. 102—103°/15 mm., n_D^{20} 1·4061 (Found : P, 17·0. Calc. for $C_6H_{15}O_4P$: P, 17·0%).

The solvent used in the kinetic runs was the best grade of ether, and was distilled from sodium before use.

Method and Appartus.—Hydrogen bromide and the phosphonate in ethereal solution were allowed to react in a thermostat. A solution of hydrogen bromide was first prepared by passing the dry gas into the ether, and the approximate concentration of the solution was determined. This stock solution was then diluted with more solvent, to a known volume, to give approximately the concentration required, and its exact molarity determined. The stoicheiometrically equivalent weight of ester and the final molarities were calculated, after allowance for the volume change on the addition of the ester. Samples were removed after specified time intervals, by the application of dried air under pressure to the surface of the solution. The solution was forced up an exit tube, through a tap, and into a sampler of known volume, also fitted with taps at each end. The bromide ion, in the aqueous extract of each sample, was determined by Volhard's method.

Results.—Three typical runs are reported in Tables 1, 4, and 6.

TABLE 1.	(a) Diethyl	ethylphosphonate	(0.1605м)	and hydrogen	bromide	(0.3205м)) at 25.0° .
----------	-------------	------------------	-----------	--------------	---------	-----------	-----------------------

Time (min.) HBr concn. $(10^{-3} \text{ mole } 1.^{-1})$	$2 \\ 318.5$	$15 \\ 302 \cdot 5$	30 $283\cdot 5$	$\begin{array}{c} 60\\261 \end{array}$	100 238	$180 \\ 206.5$
Time (min HBr concn. (10 ⁻³ mole l. ⁻¹)	$\begin{array}{c} 245 \\ 190 \end{array}$	320 176·5	408 166	$\begin{array}{c} 1360 \\ 118 \end{array}$	$\frac{1682}{112}$	2757 96
Time (min.) HBr concn. (10 ⁻³ mole l. ⁻¹)	$\begin{array}{r} 4290 \\ 76 \end{array}$	$\begin{array}{c} 6075\\ 63 \end{array}$	$8360 \\ 49.5$	9840 46		

(a) (See Table 1.) From the smooth curve drawn on a large scale through the experimental points, the hydrogen bromide concentrations at equal intervals of time were read for the first half of the complete reaction. The corresponding ester concentrations were calculated, neglecting the second reaction, and a graph of log ([HBr]/[Ester]) versus time was plotted. The data in Table 2 were thus used.

			TABLE 2.				
Time (min.) log ([HBr]/[Ester])	0 0·300	$\begin{array}{c} 20 \\ 0.339 \end{array}$	$\begin{array}{c} 40\\0{\cdot}378\end{array}$	60 0·412	80 0·448	$\begin{array}{c} 100 \\ 0.485 \end{array}$	$\begin{array}{c} 120 \\ 0{\cdot}521 \end{array}$
Time (min.) log ([HBr]/[Ester])	140 0∙559	160 0·601	180 0·646	$\begin{array}{c} 220\\0{\cdot}741 \end{array}$	$\begin{array}{c} 260 \\ 0{\cdot}843 \end{array}$	$\begin{array}{c} 300 \\ 0.958 \end{array}$	340 1·094

From the initially linear slope, k_1 (the second-order specific rate for the first dealkylation) was calculated to be 4.43×10^{-4} l. mole⁻¹ sec.⁻¹. A curve of hydrogen bromide concentration versus time was also drawn for the whole reaction, and hydrogen bromide concentrations at larger time intervals read off. A graph of log 1/[HBr] versus time was plotted (see Table 3).

			T.	ABLE 3						
Time (min.) 1/[HBr] (l. mole ⁻¹)	500 1 6·33 7	000 2 769 9	600)• 4 0	3000 11·0	$4000 \\ 12.7$	$5000 \\ 14.3$	$\begin{array}{c} 6000\\ 15\cdot 9\end{array}$	$7000 \\ 17.5$	8000 19·4	$9000 \\ 20.8$
TABLE 4. (b) <i>Diethy</i>	l n-octy	elphosj 0 ·146 0	bhonate Эм) at :	e (0·073 25·0°.	80м) ан	d hydro	ogen bro	omide	
Time (min.) HBr concn. (10 ⁻³ mole l.	3 -1) 145	$16 \\ 140.5$	$\begin{array}{c} 40\\133\end{array}$	$\begin{array}{c} 86 \\ 122 \end{array}$	$\begin{array}{c} 147 \\ 115 \end{array}$	$\begin{array}{c} 206 \\ 107 \cdot 5 \end{array}$	$\begin{array}{c} 250 \\ 104 \end{array}$	305 100	380 95	460 91
Time (min.) HBr concn. (10 ⁻³ mole l. ⁻	1182 -1 72.5	$1408 \\ 70.5$	$\begin{array}{c} 1825\\ 67\end{array}$	$3085 \\ 59.5$	$5850 \\ 51.5$	8630 45	14,620 39	20,150 33	$\begin{array}{r} 24,750\\31 \end{array}$	

The slope of the linear part of this curve was equal to k_2 (the second-order specific rate for the second dealkylation) = 2.65×10^{-5} l. mole⁻¹ sec.⁻¹. The ratio k_1/k_2 was thus 16.7.

			T.	ABLE 5.					
Time (min.) log ([HBr]/[Ester])	$\begin{array}{c} 0\\ 0{\cdot}301 \end{array}$	$\begin{array}{c} 20 \\ 0 \cdot 325 \end{array}$	60 0·365	100 0·401	140 0·433	180 0·468	$\begin{array}{c} 220 \\ 0{\cdot}503 \end{array}$	$\begin{array}{c} 260 \\ 0{\boldsymbol{\cdot}}536 \end{array}$	300 0∙570
Time (min.) log ([HBr]/[Ester])	340 0- 6 03	380 0·637	420 0·670	460 0·698					
Time (min.) 1/[HBr] (1. mole ⁻¹)	$\begin{array}{c} 2000 \\ \mathbf{15\cdot2} \end{array}$	4000 17·7	6000 19·4	$\begin{array}{c} 8000\\ 20{\cdot}8 \end{array}$	$\begin{array}{c} 10,000 \\ 22.2 \end{array}$	$12,000 \\ 23.6$	$14,000 \\ 25.0$	$18,000 \\ 28.2$	$22,000 \\ 30.8$

(b) (See Table 4.) Graphs of log [HBr]/[Ester] and 1/[HBr] versus time were plotted as before, with the results given in Table 5. The value of k_1 was 4.45×10^{-4} and of $k_2 1.22 \times 10^{-5}$ l. mole⁻¹ sec.⁻¹. The ratio k_1/k_2 in this case was 36.5, and hence the deviation from linearity of the log [HBr]/[Ester] plot develops much later.

TABLE 6. (c) Dieth	vyl acety	lphosphon	ate (0·10	95м) and	hydrogen	bromide	(0.2180м)	at 25.0°.
Time (min.) $\alpha = [HBr]/[H$	Br] ₀	2 0·996	$\begin{array}{c} 17 \\ 0.985 \end{array}$	30 ()•969	69 0·940	$\begin{array}{c} 131 \\ 0{\cdot}892 \end{array}$	197 0·849	$\begin{array}{c} 275 \\ 0.792 \end{array}$	351 0·732
Time (min.) $\alpha = [HBr]/[H$	Br] ₀	44 5 0∙691	504 0·678	1400 0·429	$1715 \\ 0.383$	2025 0 ·346	$2810 \\ 0.275$	4290 0·188	5970 0·141

(c) (See Table 6.) α versus time was plotted on a large scale, and times of 20% up to 60% reaction were read. The "t" ratios were calculated and by interpolation in the prepared tables of Frost and Schwemer the corresponding values of $1/\kappa$ were found. From the average $1/\kappa$ value, the values of τ were also found from the tables, and k_1 and hence k_2 were calculated. Results are in Tables 7 and 8.

TABLE 7.

Reaction (%) 20 30 40	t (min.) 265 450 715	Percentage compared 60/20 60/30 60/40	" _t " ratio 6·038 3·556 2·248	1/κ 2·046 2·145 2·000	Reaction (%) 50 60	t (min.) 1063 1600	Percentage compared 60/50 50/20 50/30	"t" ratio 1·506 4·012 2·363	$1/\kappa$ 2.092 2.030 2.181
				Average 1	$1/\kappa = 2.08$				

	Tabli	Е 8 .			
Reaction (%)	20	30	40	50	60
au	0.2510	0.4311	0.6727	1.012	1.523
$10^{-4}k_1$ (l. mole ⁻¹ sec. ⁻¹)	1.446	1.462	1.436	1.453	1.453
Average $k_1 = 1.45 \times$	10-4 l. mo	le ⁻¹ sec. ⁻¹ .			
Average $k_1 = 1.45 \times$	$10^{-4}/2.08$	$= 6.97 \times 10^{-1}$	⁻⁵ l. mole⁻¹ se	c1.	

The rate constants obtained for the various esters, in ethereal solution, are summarised in Table 9.

TABLE 9.

	Initial (mole	concn. e l. ⁻¹)	Rate con (l. mole ⁻¹		
Ester	HBr	Ester	$10^{4}k_{1}$	$10^{5}k_{2}$	$k_1/k_2 *$
Et·PO ₃ Et ₂	0·3205, 0·1485 0·1880, 0·0710	0·1605, 0·0750 0·0940, 0·0355	$ \begin{array}{r} 4\cdot 43, 4\cdot 27 \\ 4\cdot 26, 4\cdot 33 \end{array} $	2.65, 2.50 2.35, 2.64	17.2
Et ₂ HPO ₃	0.3945, 0.2400	0.1970, 0.1200	4.73, 4.45	3.44, 3.50	13.1
$n-C_{B}H_{17}$ ·PO ₃ Et ₃	0.1340, 0.1460	0.0670, 0.0730	4.30, 4.45	1.31, 1.22	34
CHPhMe·PO ₃ Et ₂	0.2070, 0.1270	0.1070, 0.0635	3 37, 3 07	1.38, 1.33	23
Ac PO ₃ Et ₂	0.1960, 0.2180	0.0980, 0.1095	1.37, 1.45	6.56, 6.97	$2 \cdot 1$
Et·PO ₃ Pr ⁿ	0.3045, 0.1895	0.1525, 0.0950	3.56, 3.78	1.23, 1.31	28
Et PO ₃ Pri	0.2200, 0.1380	0.1105, 0.0690	0.933, 0.98 6	0.880, 0.917	10.7
Et ₃ PO ₄	0.1710	0.0855	9.02	7.13	12.7
Et, HPO, at 15.0°	0.1575, 0.1540	0.0785, 0.0775	0.921, 0.924	1.72, 1.73	5.4
Et PO, Et, at 15.0°	0.1767	0.0825	1.38	0.68	20.3
Et,PO, at 15.0°	0.3130	0.1040	3.12	3 ·06	10.2
Et ₂ HPO ₃ at 20.0°	0.1100	0.0660	1.95		

* From average values of k_1 and k_2 .

DISCUSSION

In each example the dealkylation was clearly of the second order; but because the observations were all for ethereal solutions, and the influence of ether has not yet been decided, a detailed discussion on mechanism must be postponed until data for other solvents and conditions are available. It is possible that, even if competitive complex-formation between hydrogen bromide and ether did not complicate the kinetics, it might still affect the values of the rate constants. Ether was chosen because of the convenient solubility of hydrogen bromide. Nevertheless the results provide a quantitative comparison of the influence of structure on the first and the second dealkylation, and also clearly show the degree of control which may be held over the steps of dealkylation.

Replacement of hydrogen by an ethyl or *n*-octyl group in the compound O.PH(OEt)₂ has little effect on k_1 (the first dealkylation), but has more effect on k_2 (the second one), and increases the ratio k_1/k_2 . Thus for diethyl hydrogen phosphite k_1/k_2 is 13·1, for diethyl ethylphosphonate 17·2, and for diethyl *n*-octylphosphonate 34. These ratios indicate to what extent dealkylation may be restricted to the first group, and so lead to the convenient preparation of the acid esters. Ethyl hydrogen *n*-octylphosphonate, O.PR(OEt)(OH), was obtained in this way by Cooke, Gerrard, and Green (*Chem. and Ind.*, 1953, 351). In view of the great reactivity of the 1-carbon atom in 1-phenylethanol (cf. Gerrard, *J.*, 1944, 88; Gerrard and Shepherd, *J.*, 1953, 2069), the difference between k_1 (3·2 × 10⁻⁴) for diethyl 1-phenylethylphosphonate and k_1 (4·3 × 10⁻⁴) for diethyl hydrogen phosphite appears surprisingly small. The acetyl group has a more marked effect: $k_1 = 1.4 \times 10^{-4}$, but k_2 is larger than for the hydrogen phosphite, making $k_1/k_2 = 2$. For such an ester, the production of the acid ester will be very much less efficient.

Replacement of the ester ethyl group by *n*-propyl, $O:PEt(OEt)_2 \longrightarrow O:PEt(OPr^n)_2$, caused a slight reduction in k_1 , and a greater one in k_2 , thus increasing the ratio k_1/k_2 to 28. Replacement by *iso*propyl, to give $O:PEt(OPr^i)_2$, causes a considerable reduction in k_1 (0.96 $\times 10^{-4}$), but a smaller reduction in k_2 , lowering the ratio k_1/k_2 to 11.

For triethyl phosphate, k_1 and k_2 are both twice as large as for diethyl hydrogen phosphite. This could be due in some measure to the statistical availability of alkyl groups.

In the types of ester studied, the phosphorus atom is quinquevalent and of the general structure $O:PX(OR)_2$, where X = H, OR, or R, or R'; but a trialkyl phosphite, $P(OR)_3$, contains a tervalent phosphorus atom, and the much greater rate of the first dealkylation, $P(OR)_3 + HBr \longrightarrow O:PH(OR)_2 + RBr$, may be partly attributed to a tendency for phosphorus to attain quinquecovalency. It was found by Gerrard and Whitbread (*loc. cit.*) that, in 0.2m-concentration and with hydrogen bromide, tri-*n*-butyl phosphite was completely dealkylated to dibutyl hydrogen phosphite in 7 minutes at -11° . Of relevance is the fact that in the examples of alcohols of ordinary reactivity it is the dialkyl hydrogen phosphite, and never the trialkyl phosphite, which can be obtained by the interaction of the alcohol and phosphorus trichloride.

We thank Dr. W. F. Watson for helpful discussions.

THE NORTHERN POLYTECHNIC, HOLLOWAY ROAD, LONDON, N.7.

[Received, February 7th, 1955.]